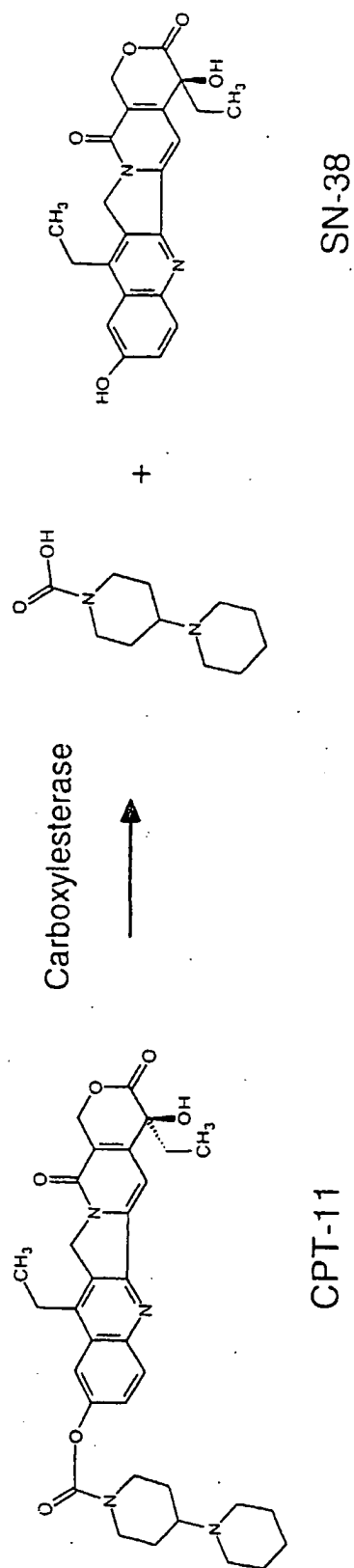
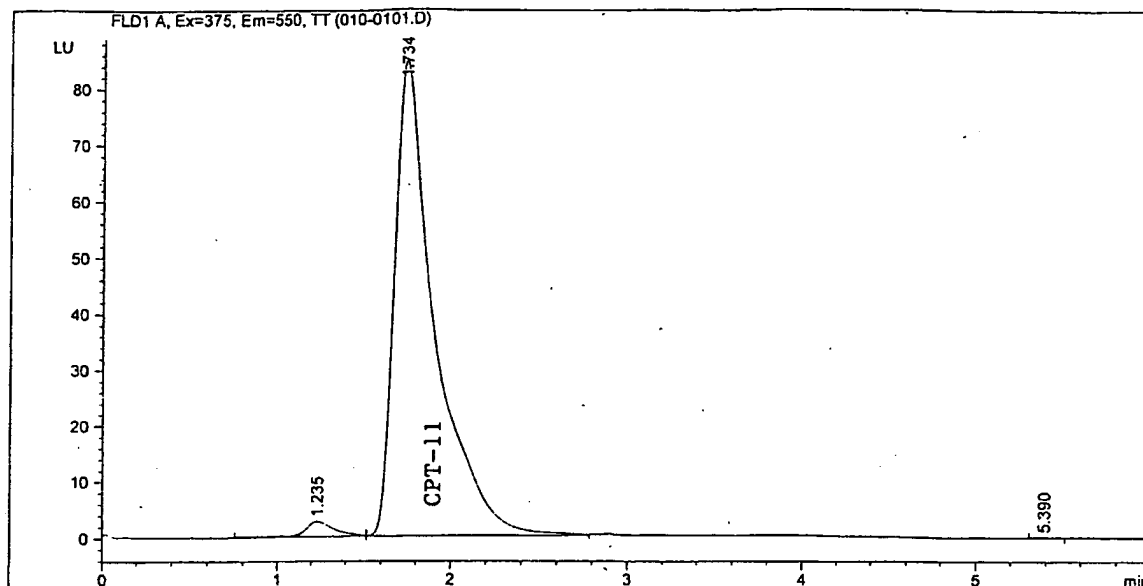


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FIGURE 2



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=====  
Area Percent Report  
=====

Sorted By : Signal  
Multiplier : 1.0000  
Dilution : 1.0000

Signal 1: FLD1 A, Ex=375, Em=550, TT

Peak #	RetTime [min]	Type	Width [min]	Area LU	Area *s	Height [LU]	Area %
1	1.235	BV	0.1798	33.54967		2.69549	2.4019
2	1.734	VB	0.2291	1362.90149		84.52777	97.5726
3	5.390	PP	0.0644	3.55984e-1		8.81600e-2	0.0255

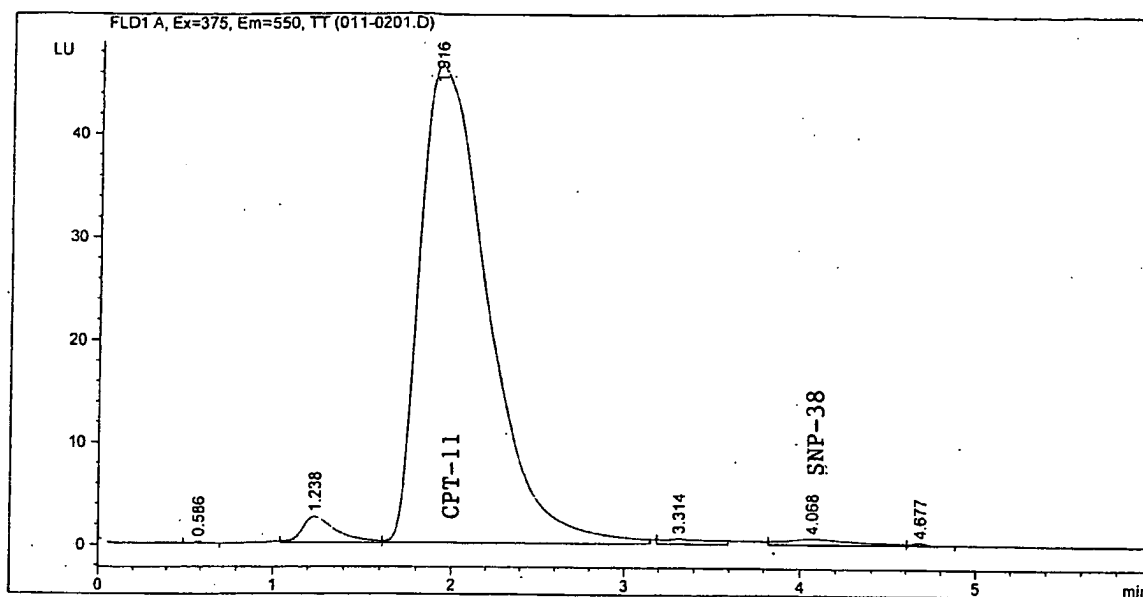
Totals : 1396.80714 87.31142

Results obtained with enhanced integrator!

=====  
\*\*\* End of Report \*\*\*  
=====

FIGURE 3

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=====  
 Area Percent Report  
 =====

Sorted By : Signal  
 Multiplier : 1.0000  
 Dilution : 1.0000

Signal 1: FLD1 A, Ex=375, Em=550, TT

Peak #	RetTime [min]	Type	Width [min]	Area LU	Area *s	Height [LU]	Area %
1	0.586	PP	0.0648	6.38727e-1	1.56677e-1	0.0482	
2	1.238	BV	0.2010	33.95303	2.51082	2.5614	
3	1.916	VB	0.4205	1261.66895	46.46422	95.1804	
4	3.314	BB	0.2377	10.32978	5.46781e-1	0.7793	
5	4.068	BV	0.4015	16.96264	5.87734e-1	1.2797	
6	4.677	VB	0.1161	2.00295	2.41638e-1	0.1511	

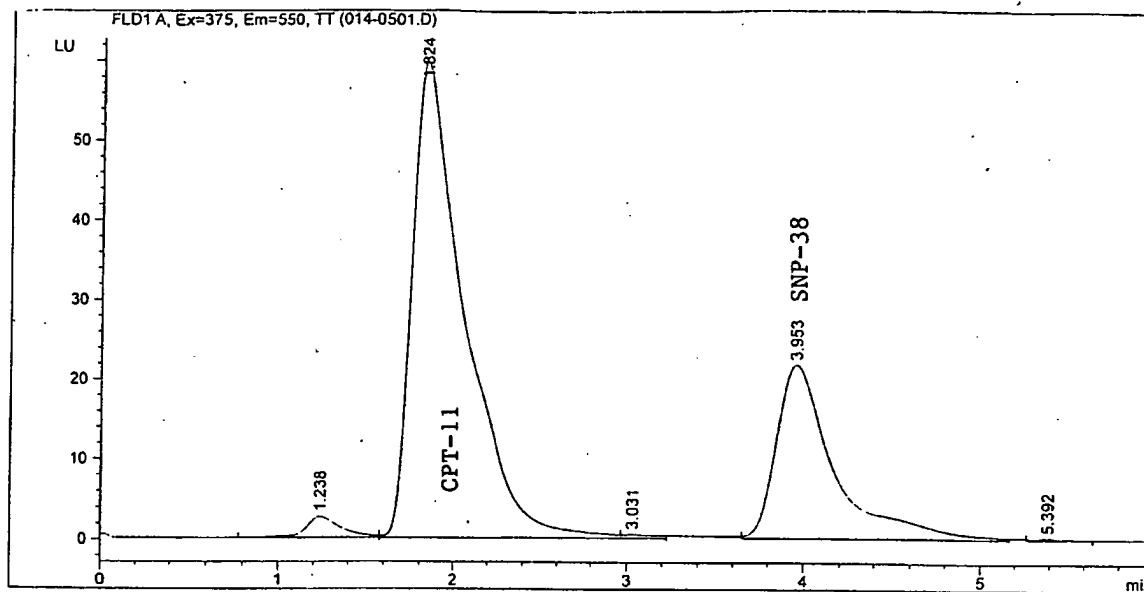
Totals : 1325.55607 50.50786

Results obtained with enhanced integrator!

=====  
 \*\*\* End of Report \*\*\*

FIGURE 4

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=====  
 Area Percent Report  
 =====

Sorted By : Signal  
 Multiplier : 1.0000  
 Dilution : 1.0000

Signal 1: FLD1 A, Ex=375, Em=550, TT

Peak #	RetTime [min]	Type	Width [min]	Area LU	Area *s	Height [LU]	Area %
1	1.238	BV	0.2036	37.44498		2.65213	2.0899
2	1.824	VV	0.2933	1256.83813		59.65673	70.1479
3	3.031	VB	0.1566	6.12651		5.05245e-1	0.3419
4	3.953	BB	0.3270	488.97583		21.75457	27.2912
5	5.392	BB	0.1365	2.31119		2.26240e-1	0.1290

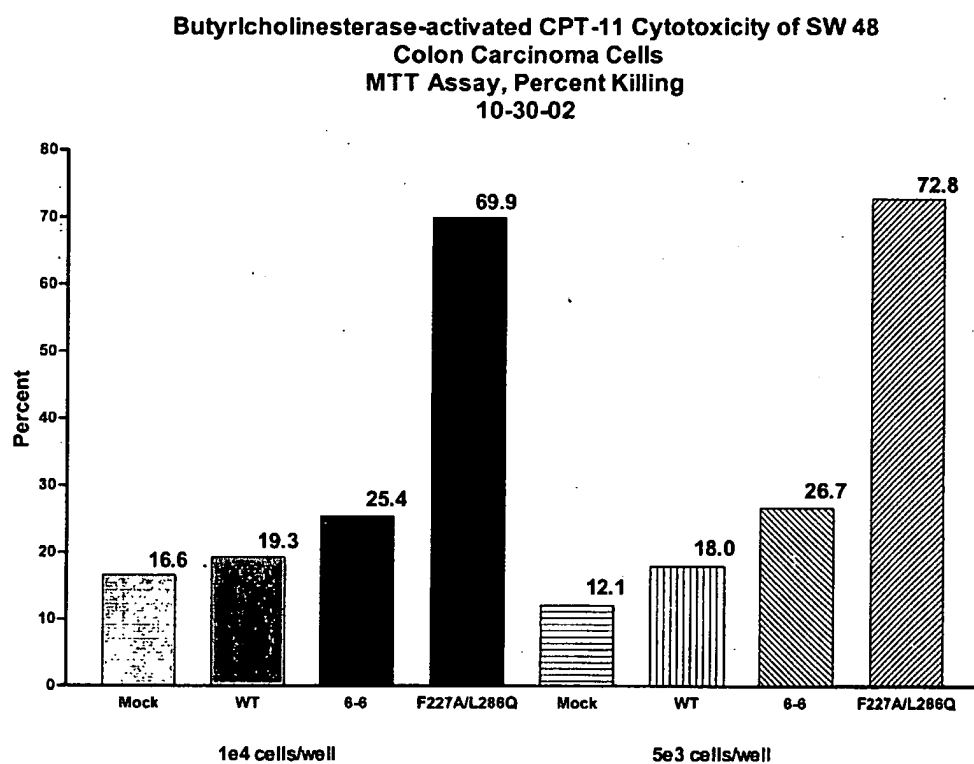
Totals : 1791.69665 84.79490

Results obtained with enhanced integrator!

=====  
 \*\*\* End of Report \*\*\*

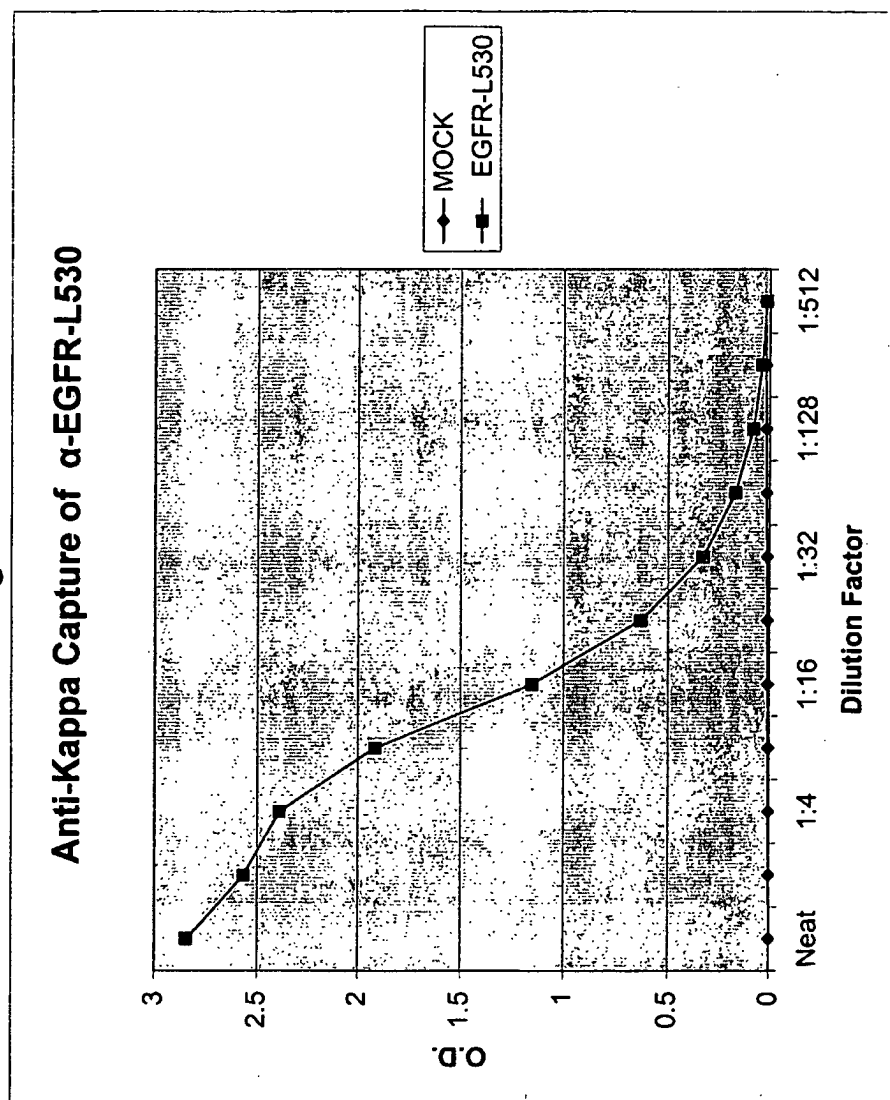
FIGURE 5

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**Figure 6**

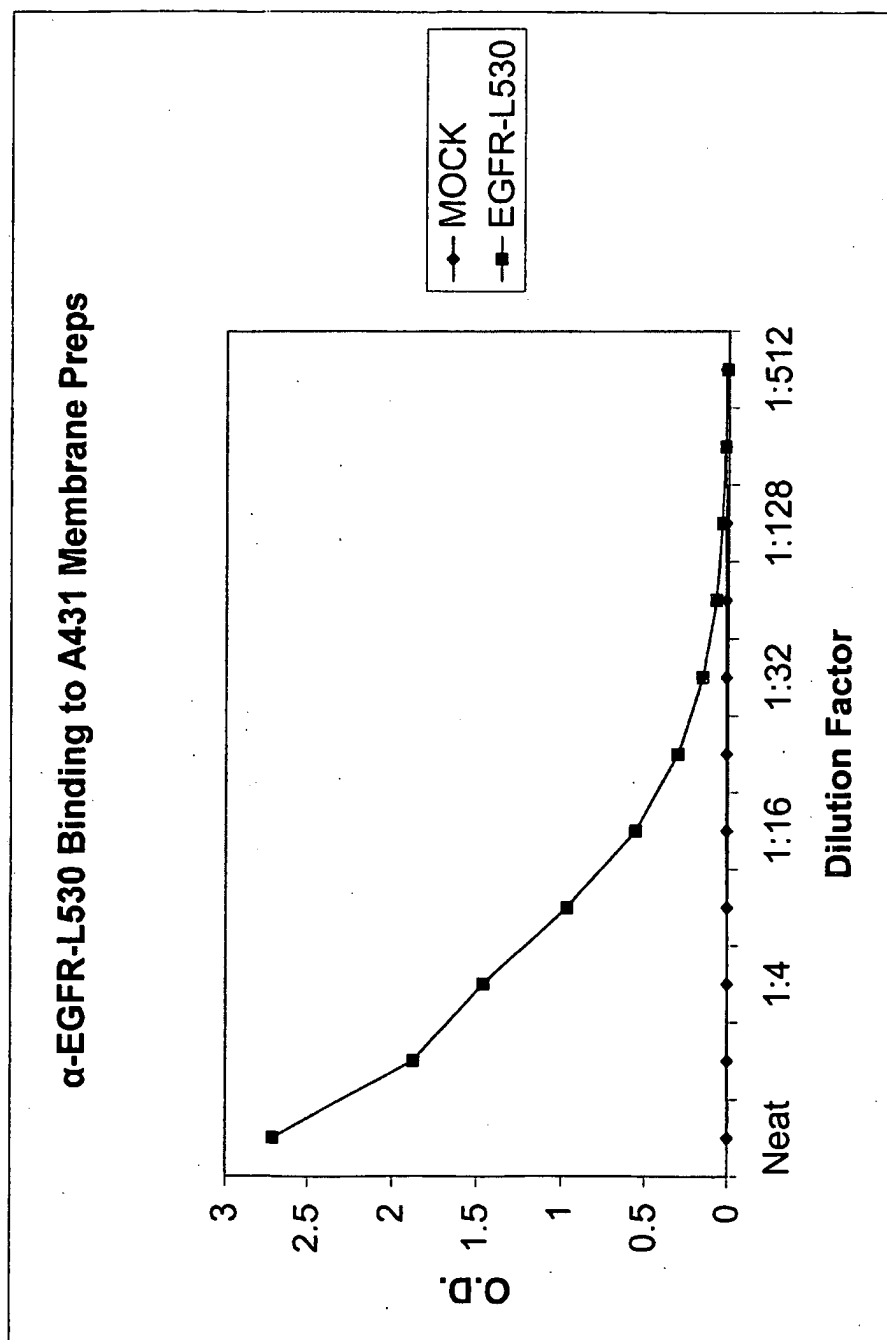
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Figure 7



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Figure 8





Mouse- $\alpha$ EGF VL construct[illegible]

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Figure 9 (continued)

613	CTG AGC AAA GCA GAC TAC GAG AAA CAC AAA GTC TAC GCC TGC GAA GTC ACC
	H Q G L S S P V T K S F N R G E C
664	CAT CAG GGC CTG AGC TCG CCC GTC ACA AAG AGC TTC AAC AGG GGA GAG TGT
	* TAG
715	

Mouse  $\alpha$ EGF-VH-CH1hingecysL530

	SEQ ID NO:	20	M	G	W	S	C	I	I	L	F	L	V	A	T	A	T
1	SEQ ID NO:	19	ATG	GGA	TGG	AGC	TGT	ATC	ATC	CTC	TTC	TTG	GTA	GCA	ACA	GCT	ACA
		G	V	H	S	Q	V	Q	L	K	Q	S	G	P	G	L	V
52		GGT	GTC	CAC	TCC	CAG	GTG	CAG	CTG	AAG	CAG	TCA	GGA	CCT	GGC	CTA	GTG
		P	S	Q	S	L	S	I	T	C	T	V	S	G	F	S	L
103		CCC	TCA	CAG	AGC	CTG	TCC	ATC	ACC	TGC	ACA	GTC	TCT	GGT	TTC	TCA	TTA
		N	Y	G	V	H	W	V	R	Q	S	P	G	K	G	L	E
154		AAC	TAT	GGT	GTA	CAC	TGG	GTT	CGC	CAG	TCT	CCA	GGA	AAG	GGT	CTG	GAG
		L	G	V	I	W	S	G	G	N	T	D	Y	N	T	P	F
205		CTG	GGA	GTG	ATA	TGG	AGT	GGT	GGA	AAC	ACA	GAC	TAT	AAT	ACA	CCT	TTC
		S	R	L	S	I	N	K	D	N	S	K	S	Q	V	F	K
2256		TCC	AGA	CTG	AGC	ATC	AAC	AAG	GAC	AAT	TCC	AAG	AGC	CAA	GTT	TTC	TTT
		M	N	S	L	Q	S	N	D	T	A	I	Y	Y	C	A	R
307		ATG	AAC	AGT	CTG	CAA	TCT	AAT	GAC	ACA	GCC	ATA	TAT	TAC	TGT	GCC	AGA
		L	T	Y	Y	D	Y	E	F	A	Y	W	G	Q	G	T	L
358		CTC	ACC	TAC	TAT	GAT	TAC	GAG	TTT	GCT	TAC	TGG	GGC	CAA	GGG	ACT	CTG
		T	V	S	A	A	S	T	K	G	P	S	V	F	P	L	A
409		ACT	GTC	TCT	GCA	GCC	TCC	ACC	AAG	GGC	CCA	TCG	GTC	TTC	CCC	CTG	GCA
		S	S	K	S	T	S	G	G	T	A	A	L	G	C	L	V
460		TCC	TCC	AAG	AGC	ACC	TCT	GGG	GGC	ACA	GCG	GCC	CTG	GGC	TGC	CTG	GTC
		D	Y	F	P	E	P	V	T	V	S	W	N	S	G	A	L
511		GAC	TAC	TTC	CCC	GAA	CCG	GTG	ACG	GTG	TCG	TGG	AAC	TCA	GGC	GCC	CTG
		S	G	V	H	T	F	P	A	V	L	Q	S	S	G	L	Y
562		AGC	GGC	GTG	CAC	ACC	TTC	CCG	GCT	GTC	CTA	CAG	TCC	TCA	GGA	CTC	TAC
		L	S	S	V	V	T	V	P	S	S	S	L	G	T	Q	T

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Figure 10 (continued)

613	CTC AGC AGC GTG GTG ACC GTG CCC TCC AGC AGC TTG GGC ACC CAG ACC TAC
664	ATC TGC AAC GTG AAT CAC AAG CCC AGC AAC ACC AAG GTG GAC AAG AAA GCA
715	GAG CCC AAA TCT TGT GAC AAA ACT CAC ACA TGT CCA CCG TGT CCA AAG CTT
766	GAA GAT GAC ATC ATA ATT GCA ACA AAG AAT GGA AAA GTC AGA GGG ATG AAC
817	TTG ACA GTT TTT GGT GGC ACG GTA ACA GCC TTT CTT GGA ATT CCC TAT GCA
868	CAG CCA CCT CTT GGT AGA CTT CGA TTC AAA AAG CCA CAG TCT CTG ACC AAG
919	TGG TCT GAT ATT TGG AAT GCC ACA AAA TAT GCA AAT TCT TGC TGT CAG AAC
970	ATA GAT CAA AGT TTT CCA GGC TTC CAT GGA TCA GAG ATG TGG AAC CCA AAC
1021	ACT GAC CTC AGT GAA GAC TGT TTA TAT CTA AAT GTA TGG ATT CCA GCA CCT
1072	AAA CCA AAA AAT GCC ACT GTA TTG ATA TGG ATT TAT GGT GGT TTT CAA
1123	ACT GGA ACA TCA TCT TTA CAT GTT TAT GAT GGC AAG TTT CTG GCT CGG GTT
1174	GAA AGA GTT ATT GTA GTG TCA ATG AAC TAT AGG GTG GGT GCC CTA GGA TTC
1225	TTA GCT TTG CCA GGA AAT CCT GAG GCT CCA GGG AAC ATG GGT TTA TTT GAT
1276	CAA CAG TTG GCT CTT CAG TGG GTT CAA AAA AAT ATA GCA GCC TTT GGT GGA

Figure 10 (continued)

1327	AAT CCT AAA AGT GTA ACT CTC TTT GGA GAA AGT GCA GGA GCA GCT TCA GTT
1378	S L H L L S P G S H S L F T R A I
1429	AGC CTG CAT TTG CTT TCT CCT GGA AGC CAT TCA TTG TTC ACC AGA GCC ATT
1480	L Q S G S F N A P W A V T S L Y E
1531	CTG CAA AGT GGT TCC TTT AAT GCT CCT TGG GCG GTA ACA TCT CTT TAT GAA
1582	A R N R T L N L A K L T G C S R E
1633	GCT AGG AAC AGA ACG TTG AAC TTA GCT AAA TTG ACT GGT TGC TCT AGA GAG
1684	N E T E I I K C L R N K D P Q E I
1735	AAT GAG ACT GAA ATA ATC AAG TGT CTT AGA AAT AAA GAT CCC CAA GAA ATT
1786	L L N E A F V V P Y G T P L S V N
1837	CTT CTG AAT GAA GCA TTT GTT GTC CCC TAT GGG ACT CCT TTG TCA GTA AAC
1888	F G P T V D G D F L T D M P D I L
1939	TTT GGT CCG ACC GTG GAT GGT GAT TTT CTC ACT GAC ATG CCA GAC ATA TTA
1990	L E L G Q F K K T Q I L V G V N K
	CTT GAA CTT GGA CAA TTT AAA ACC CAG ATT TTG GTG GGT GTT AAT AAA
	D E G T A F L V Y G A P G F S K D
	GAT GAA GGG ACA GCT TTT TTA GTC TAT GGT GCT CCT GGC TTC AGC AAA GAT
	N N S I I T R K E F Q E G L K I F
	AAC AAT AGT ATC ATA ACT AGA AAA GAA TTT CAG GAA GGT TTA AAA ATA TTT
	F P G V S E F G K E S I L F H Y T
	TTT CCA GGA GTG AGT GAG TTT GGA AAG GAA TCC ATC CTT TTT CAT TAC ACA
	D W V D D Q R P E N Y R E A L G D
	GAC TGG GTA GAT GAT CAG AGA CCT GAA AAC TAC CGT GAG GCC TTG GGT GAT
	V V G D Y N F I C P A L E F T K K
	GTT GTT GGG GAT TAT AAT TTC ATA TGC CCT GCC TTG GAG TTC ACC AAG AAG
	F S E W G N N A F F Y F E H R S
	TTC TCA GAA TGG GGA AAT AAT GCC TTT TTC TAC TAT TTT GAA CAC CGA TCC
	S K L P P W P E W M G V M H G Y E I

Figure 10 (continued)

2041	TCC AAA CTT CCG TGG CCA GAA TGG ATG GGA GTG ATG CAT GGC TAT GAA ATT
	E F V G F L P L E R R D N Y T K A
2092	GAA TTT GTC TTT GGT TTA CCT CTG GAA AGA AGA GAT AAT TAC ACA AAA GCC
	E E I L S R S I V K R W A N F A K
2143	GAG GAA ATT TTG AGT AGA TCC ATA GTG AAA CGG TGG GCA AAT TTT GCA AAA
	Y G N P N E T Q N N S T S W P V F
2194	TAT GGG AAT CCA AAT GAG ACT CAG AAC AAT AGC ACA AGC TGG CCT GTC TTC
	K S T E Q K Y L T L N T E S T R I
2245	AAA AGC ACT GAA CAA AAA TAT CTA ACC TTG AAT ACA GAG TCA ACA AGA ATA
	M T K L R A Q Q C R F W T S F F P
2296	ATG ACG AAA CTA CGT GCT CAA CAA TGT CGA TTC TGG ACA TCA TTT TTT CCA
	K V *
2347	AAA GTC TGA

Figure 11

```

E D D I I I I A T K N G K V R G M N
1 GAA GAT GAC ATC ATA ATT GCA ACA AAG AAT GGA AAA GTC AGA GGG ATG AAC
L T V F G G G T V T A F L G I P Y A
52 TTG ACA GTT TTT GGT GGC ACG GTA ACA GCC TTT CTT GGA ATT CCC TAT GCA
Q P P L G R L R F K K P Q S L T K
103 CAG CCA CCT CTT GGT AGA CTT CGA TTC AAA AAG CCA CAG TCT CTG ACC AAG
W S D I W N A T K Y A N S C C Q N
154 TGG TCT GAT ATT TGG AAT GCC ACA AAA TAT GCA AAT TCT TGC TGT CAG AAC
I D Q S F P P CCA GGC TTC CAT GGA TCA GAG ATG TGG AAC CCA AAC
205 ATA GAT CAA AGT TTT CCA GGC TTC CAT GGA TCA GAG ATG TGG AAC CCA AAC
T D L S E D C L Y L N V W I P A P
256 ACT GAC CTC AGT GAA GAC TGT TTA TAT CTA AAT GTA TGG ATT CCA GCA CCT
K P K N A T V L I W I Y G G F Q
307 AAA CCA AAA AAT GCC ACT GTA TTG ATA TGG ATT TAT GGT GGT TTT CAA
T G T S S L H V Y D G K F L A R V
358 ACT GGA ACA TCA TCT TTA CAT GTT TAT GAT GGC AAG TTT CTG GCT CGG GTT
E R V I V V S M N Y R V G A L G F
409 GAA AGA GTT ATT GTA GTG TCA ATG AAC TAT AGG GTG GGT GCC CTA GGA TTC
L A L P G N P E A P G N M G L F D
460 TTA GCT TTG CCA GGA AAT CCT GAG GCT CCA GGG AAC ATG GGT TTA TTT GAT
Q Q L A L Q W V Q K N I A A F G G
511 CAA CAG TTG GCT CTT CAG TGG GTT CAA AAA AAT ATA GCA GCC TTT GGT GGA
N P K S V T L F G E S A G A S V
562 AAT CCT AAA AGT GTA ACT CTC TTT GGA GAA AGT GCA GGA GCT TCA GTT
S L H L L S P G S H S L F T R A I
613 AGC CTG CAT TTG CTT TCT CCT GGA AGC CAT TCA TTG TTC ACC AGA GCC ATT
L Q S G S F A P W A V T S L Y E

```

Figure 11 (continued)

664 CTG CAA AGT GGT TCC TTT AAT GCT CCT TGG GCG GTA ACA TCT CTT TAT GAA  
 A R N R T L N L A K L T G C S R E  
 715 GCT AGG AAC AGA ACG TTG AAC TTA GCT AAA TTG ACT GGT TGC TCT AGA GAG  
 N E T E I I K C L R N K D P Q E I  
 766 AAT GAG ACT GAA ATA ATC AAG TGT CTT AGA AAT AAA GAT CCC CAA GAA ATT  
 L L N E A F V V P Y G T P L S V N  
 817 CTT CTG AAT GAA GCA TTT GTT GTC CCC TAT GGG ACT CCT TTG TCA GTA AAC  
 F G P T V D G D F L T D M P D I L  
 868 TTT GGT CCG ACC GTG GAT GGT GAT TTT CTC ACT GAC ATG CCA GAC ATA TTA  
 L E L G Q F K K T Q I L V G V N K  
 919 CTT GAA CTT GGA CAA TTT AAA AAA ACC CAG ATT TTG GTG GGT GTT AAT AAA  
 D E G T A F L V Y G A P G F S K D  
 970 GAT GAA GGG ACA GCT TTT TTA GTC TAT GGT GCT CCT GGC TTC AGC AAA GAT  
 N N S I I T R K E F Q E G L K I F  
 1021 AAC AAT AGT ATC ATA ACT AGA AAA GAA TTT CAG GAA GGT TTA AAA ATA TTT  
 F P G V S E F G K E S I L F H Y T  
 1072 TTT CCA GGA GTG AGT GAG TTT GGA AAG GAA TCC ATC CTT TTT CAT TAC ACA  
 D W V D D Q R P E N Y R E A L G D  
 1123 GAC TGG GTA GAT GAT CAG AGA CCT GAA AAC TAC CGT GAG GCC TTG GGT GAT  
 V V G D Y N F I C P A L E F T K K  
 1174 GTT GTT GGG GAT TAT AAT TTC ATA TGC CCT GCC TTG GAG TTC ACC AAG AAG  
 F S E W G N N A F F Y Y F E H R S  
 1225 TTC TCA GAA TGG GGA AAT AAT GCC TTT TTC TAC TAT TTT GAA CAC CGA TCC  
 S K L P W P E W M G V M H G Y E I  
 1276 TCC AAA CTT CCG TGG CCA GAA TGG ATG GTG ATG CAT GGC TAT GAA ATT  
 E F V F G L P L E R R D N Y T K A  
 1327 GAA TTT GTC TTT GGT TTA CCT CTG GAA AGA AGA GAT AAT TAC ACA AAA GCC  
 E E I L S R S I V K R W A N F A K



Figure 11 (continued)

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1378 GAG GAA ATT TTG AGT AGA TCC ATA GTG AAA CGG TGG GCA AAT TTT GCA AAA
      Y G N P N E T Q N N S T S W P V F
1429 TAT GGG AAT CCA AAT GAG ACT CAG AAC AAT AGC ACA AGC TGG CCT GTC TTC
      K S T E Q K Y L T L N T E S T R I
1480 AAA AGC ACT GAA CAA AAA TAT CTA ACC TTG AAT ACA GAG TCA ACA AGA ATA
      M T K L R A Q Q C R F W T S F F P
1531 ATG ACG AAA CTA CGT GCT CAA CAA TGT CGA TTC TGG ACA TCA TTT TTT CCA
      K V L E M T G N I D E A E W E W K
1582 AAA GTC TTG GAA ATG ACA GGA AAT ATT GAT GAA GCA GAA TGG GAG TGG AAA
      A G F H R W N N Y M M D W K N Q F
1633 GCA GGA TTC CAT CGC TGG AAC AAT TAC ATG ATG GAC TGG AAA AAT CAA TTT
      N D Y T S S K K E S C V G L SEQ ID NO: 22
1684 AAC GAT TAC ACT AGC AAG AAA GAA AGT TGT GTG GGT CTC SEQ ID NO: 21

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Figure 12

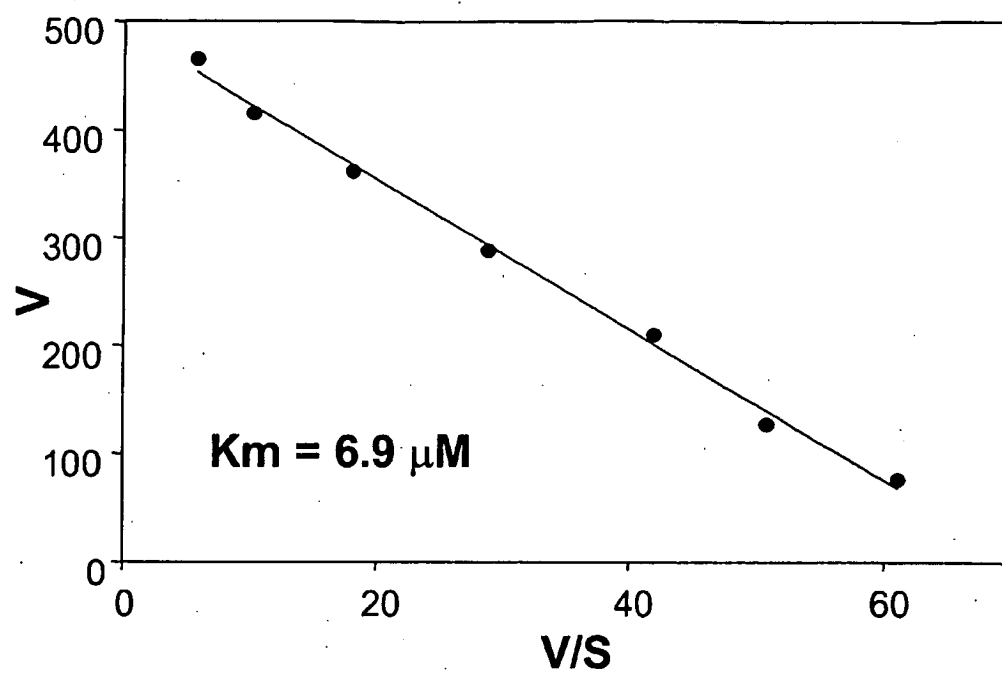
CPT-11, $\mu\text{M}$	BChE	SN38 (AUC)	SN38 / $\mu\text{g}$ BChE
2	WT	34	1.7
2	4-1	277	5,540

20	WT	269	13.5
20	4-1	927	18,540

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Figure 13



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Figure 14

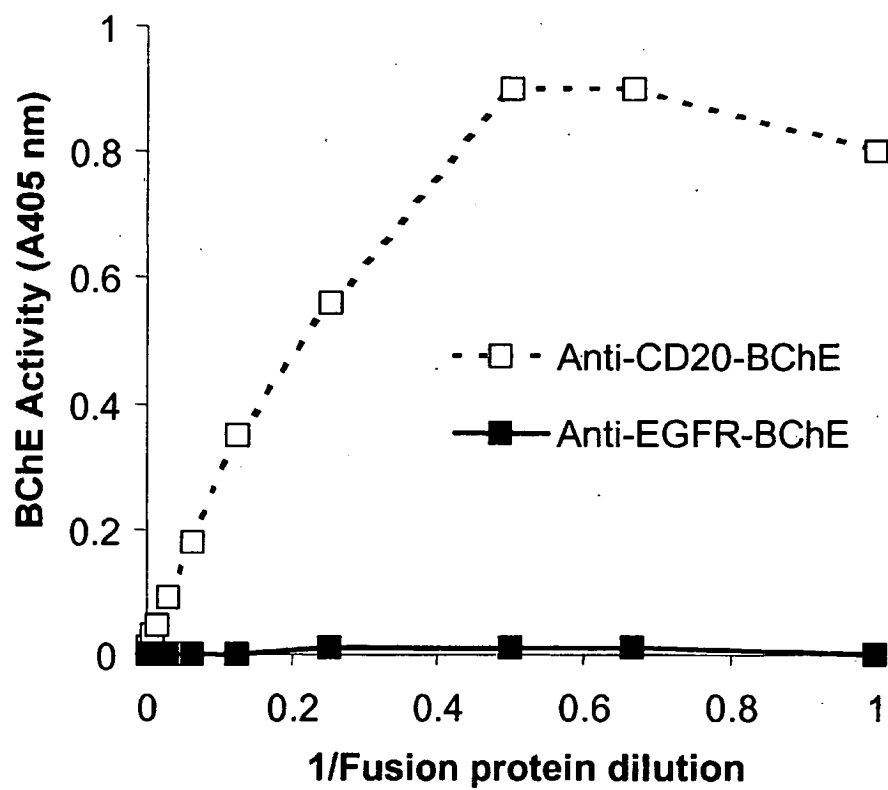
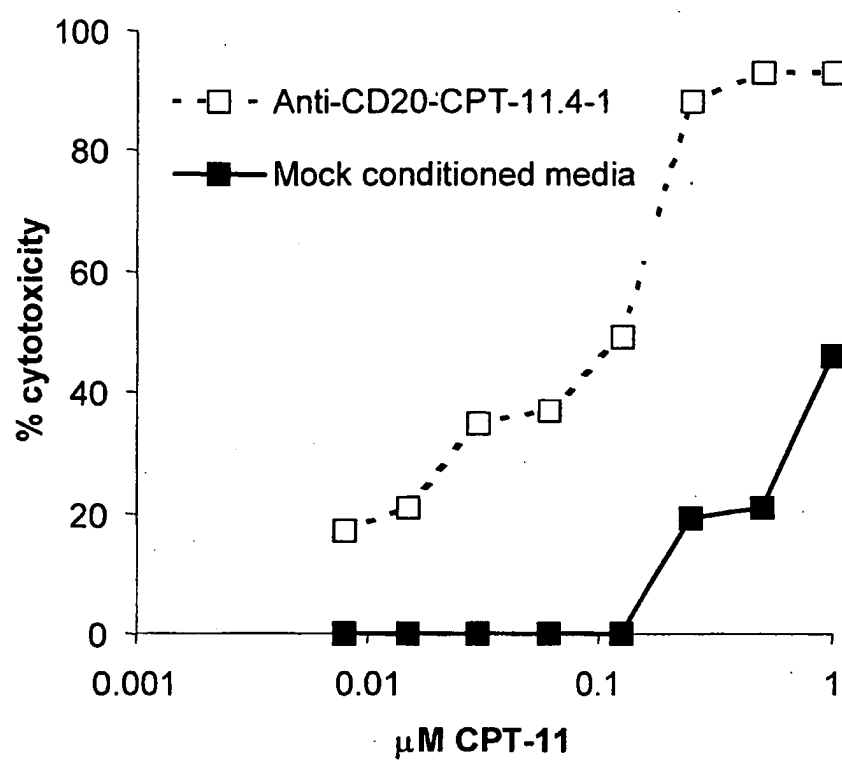


Figure 15



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Figure 16

<u>SEQ ID.NO</u>	<u>Residue #</u>	<u>wt</u>	<u>Mutation</u>	<u>Fold</u> <u>Increase</u>	<u>Assay</u>	<u>CODON</u> <u>CHANGE</u>
2	227	F	A	4	HPLC	1 TTT to GCT
		F	A	2	ONP	
		F	A	2	SW48	

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Figure 17

**F227A TEMPLATE (ALL MUTATIONS ARE ON F227A BACKGROUND)**

<u>SEQ ID.NO</u>	<u>Residue #</u>	<u>wt</u>	<u>Mutation</u>	<u>Fold Increase</u>	<u>Assay</u>		<u>CODON CHANGE</u>
24	68	N	K	80	SW48	23	AAC to AAG
26	68	N	R	75	SW48	25	AAC to CGG
28	70	D	G	12	SW48	27	GAT to GGG
30	70	D	H	65	SW48	29	GAT to CAT
32	77	H	F	75	SW48	31	CAT to TTC
34	77	H	P	80	SW48	33	CAT to CCT
36	120	T	W	100	HPLC	35	ACT to TGG
		T	W	20	SW48		
38	120	T	Y	20	SW48	37	ACT to TAT
		T	Y	80	HPLC		
40	282	Y	G	3	SW48	39	TAT to GGT
42	282	Y	N	3	SW48	41	TAT to AAT
4	284	T	A	7	HPLC	3	ACT to GCG
44	284	T	N	2	ONP	43	ACT to AAC
46	284	T	P	3	ONP	45	ACT to CCT
48	284	T	R	3	ONP	47	ACT to CGT
50	284	T	S	2	ONP	49	ACT to TCT
52	284	T	Y	2	ONP	51	ACT to TAT
54	285	P	N	4	SW48	53	CCT to AAT
56	285	P	Q	2	ONP	55	CCT to CAG
58	286	L	A	3	SW48	57	TTG to GCG
60	286	L	G	4	HPLC	59	TTG to GGG
		L	G	3	SW48		
10	286	L	H	4	HPLC	9	TTG to CAT
		L	H	3	SW48		
62	286	L	K	3	ONP	61	TTG to AAG
64	286	L	M	3	ONP	63	TTG to ATG
66	286	L	N	3	SW48	65	TTG to AAT
6	286	L	Q	3	ONP	5	TTG to CAG
		L	Q	4	SW48		
68	286	L	R	2	ONP	67	TTG to CGT
8	286	L	S	6	HPLC	7	TTG TO TCG
		L	S	2	ONP		
		L	S	5	SW48		
12	286	L	W	4	HPLC	11	TTG to TGG
		L	W	2	ONP		
70	287	S	F	6	HPLC	69	TCA to TTT
72	287	S	H	3	ONP	71	TCA to CAT
14	287	S	P	3	ONP	13	TCA to CCG

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Figure 17 (continued)

<u>SEQ ID.NO</u>	<u>Residue #</u>	<u>wt</u>	<u>Mutation</u>	<u>Fold</u> <u>Increase</u>	<u>Assay</u>		<u>CODON</u> <u>CHANGE</u>
74	287	S	R	2	ONP	73	TCA to CGT
76	287	S	T	2	ONP	75	TCA to ACT
78	327	T	A	3	SW48	77	ACA to GCT
80	327	T	P	3	SW48	79	ACA to CCT
82	329	F	L	3	SW48	81	TTT to CTT
84	330	L	S	3	SW48	83	TTA to TCG
86	331	V	A	6	SW48	85	GTC to GCG
88	331	V	G	5	SW48	87	GTC to GGT
90	331	V	P	3	SW48	89	GTC to CCT
92	331	V	S	5	SW48	91	GTC to TCT
94	331	V	T	4	SW48	93	GTC to ACT
96	332	Y	A	5	HPLC	95	TAT to GCG
98	332	Y	G	8	SW48	97	TAT to GGG
100	332	Y	L	3	SW48	99	TAT to TTG
102	332	Y	S	20	HPLC	101	TAT to TCT
		Y	S	20	SW48		
104	332	Y	W	3	SW48	103	TAT to TGG
106	429	P	K	83	SW48	105	CCG to AAG
108	429	P	L	108	SW48	107	CCG to TTG
110	429	P	Q	130	SW48	109	CCG to CAG
112	429	P	R	138	SW48	111	CCG to AGG
114	429	P	S	6	SW48	113	CCG to TCG
116	429	P	T	53	SW48	115	CCG to ACG
118	429	P	V	85	SW48	117	CCG to GTT
120	430	W	M	53	SW48	119	TGG to ATG
122	430	W	Y	120	SW48	121	TGG to TAT
124	431	P	Q	113	SW48	123	CCA to CAG
126	433	W	G	58	SW48	125	TGG to GGG
128	434	M	F	83	SW48	127	ATG to TTT
130	434	M	G	45	SW48	129	ATG to GGG
132	434	M	K	58	SW48	131	ATG to AAG
134	434	M	L	100	SW48	132	ATG to CTG
136	434	M	N	50	SW48	135	ATG to AAT
138	434	M	S	45	SW48	137	ATG to TCG
140	434	M	W	63	SW48	139	ATG to TGG
142	435	G	C	55	SW48	141	GGA to TGT
144	437	M	G	6	SW48	143	ATG to GGG
146	437	M	I	12	SW48	145	ATG to ATT
148	439	G	T	9	SW48	147	GGC to ACG
150	440	Y	A	5	SW48	149	TAT to GCT
152	440	Y	E	6	SW48	151	TAT to GAG



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Figure 17 (continued)

<u>SEQ ID.NO</u>	<u>Residue #</u>	<u>wt</u>	<u>Mutation</u>	<u>Fold</u> <u>Increase</u>	<u>Assay</u>	<u>CODON</u> <u>CHANGE</u>
154	440	Y	F	9	SW48	153 TAT to TTT
156	440	Y	G	8	SW48	155 TAT to GGT
158	440	Y	H	9	SW48	157 TAT to CAT
160	440	Y	L	12	SW48	159 TAT to TTG
162	440	Y	M	13	SW48	160 TAT to ATG
164	440	Y	N	12	SW48	161 TAT to AAT
166	440	Y	Q	13	SW48	165 TAT to CAG
168	440	Y	R	12	SW48	167 TAT to AGG
170	440	Y	S	7	SW48	169 TAT to TCT
172	440	Y	T	9	SW48	171 TAT to ACT
174	441	E	T	4	SW48	173 GAA to ACT
176	442	I	L	6	SW48	175 ATT to CTG

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Figure 18

COMBINATORIALS

<u>Residue #</u>	<u>wt</u>	<u>Mutation</u>	<u>Fold Increase</u>	<u>Assay</u>	
178 68_77_227_285_331	N_H_F_P_V	K_F_A_N_A	2500	HPLC	177 N->K AAC to AAG H->F CAT to TTT F->A TTT to GCT P->N CCT to AAT V->A GTC to GCG
180 77_227_285_331	N_H_F_P_V H_F_P_V	K_F_A_N_A F_A_N_A	300 3000	SW48 HPLC	179 H->F CAT to TTT F->A TTT to GCT P->N CCT to AAT V->A GTC to GCG
182 77_227_285_331_434	H_F_P_V H_F_P_V_M	F_A_N_A F_A_N_A_L	350 800	SW48 HPLC	181 H->F CAT to TTT F->A TTT to GCT P->N CCT to AAT V->A GTC to GCG M->L ATG to CTG
184 77_227_285_331_429	H_F_P_V_M H_F_P_V_P	F_A_N_A_L F_A_N_A_R	350 1500	SW48 HPLC	183 H->F CAT to TTT F->A TTT to GCT P->N CCT to AAT V->A GTC to GCG P->R CCG to CCG
186 77_120_227_285_331	H_F_P_V_P H_T_F_P_V	F_A_N_A_R F_W_A_N_A	400 500	SW48 SW48	185 H->F CAT to TTT T->W ACT to TGG F->A TTT to GCT P->N CCT to AAT V->A GTC to GCG
188 77_227_285_331_440	H_F_P_V_Y	F_A_N_A_Q	2000	HPLC	187 H->F CAT to TTT F->A TTT to GCT P->N CCT to AAT V->A GTC to GCG Y-> Q TAT to CAG
	H_F_P_V_Y	F_A_N_A_Q	400	SW48	

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Figure 18 (continued)

<u>Residue #</u>	<u>wt</u>	<u>Mutation</u>	<u>Fold Increase</u>	<u>Assay</u>
190 277_285_398	A_P_F	V_L_I	2	HPLC 189 A->V GCA to GTC P>L CCG to CTC F->I TTC to ATT
192 227_286_332	F_L_Y	A_G_S	600	HPLC 191 F->A TTT to GCT L->G TTG to GGG Y->S TAT to TCG
194 227_429_434	F_P_M	A_L_V	93	SW48 193 F->A TTT to GCT P->L CCG to CTC M->V ATG to GTT
196 227_285_331	F_P_V	A_N_A	500	HPLC 195 F->A TTT to GCT P->N CCT to AAT V->A GTC to GCG

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Figure 19

a-CD20 VH-CH1hingeecysL530BcHE.4-1

1	E	V	Q	L	V	Q	S	G	A	E	V	K	K	P	G	E	S
	GAG	GTG	CAG	CTG	GTG	CAG	TCT	GGA	GCA	GAG	GTG	AAA	AAG	CCC	GGG	GAG	TCT
52	L	K	I	S	C	K	G	S	G	R	T	F	T	S	Y	N	M
	CTG	AAG	ATC	TCC	TGT	AAG	GGT	TCT	GGC	CGT	ACA	TTT	ACC	AGT	TAC	AAT	ATG
103	H	W	V	R	Q	M	P	G	K	G	L	E	W	M	G	A	I
	CAC	TGG	GTG	CGC	CAG	ATG	CCC	GGG	AAA	GGC	CTG	GAG	TGG	ATG	GGG	GCT	ATT
154	Y	P	L	T	G	D	T	S	Y	N	Q	K	S	K	L	Q	V
	TAT	CCC	TTG	ACG	GGT	GAT	ACT	TCC	TAC	AAT	CAG	AAG	TCG	AAA	CTC	CAG	GTC
205	T	I	S	A	D	K	S	I	S	T	A	Y	L	Q	W	S	S
	ACC	ATC	TCA	GCC	GAC	AAG	TCC	ATC	AGC	ACC	GCC	TAC	CTG	CAG	TGG	AGC	AGC
256	L	K	A	S	D	T	A	M	Y	Y	C	A	R	S	T	Y	V
	CTG	AAG	GCC	TCG	GAC	ACC	GCC	ATG	TAT	TAC	TGT	GCG	AGA	TCG	ACT	TAC	GTG
307	G	G	D	W	Q	F	D	V	W	G	K	G	T	T	V	T	V
	GGC	GGT	GAC	TGG	CAG	TTC	GAT	GTC	TGG	GGC	AAG	GGG	ACC	ACG	GTC	ACC	GTC
358	S	A	S	T	K	G	P	S	S	V	F	P	L	A	P	S	S
	TCC	TCA	GCC	TCC	ACC	AAG	GGC	CCA	TCG	GTC	TTC	CCC	CTG	GCA	CCC	TCC	TCC
409	K	S	T	S	G	T	A	A	L	G	C	L	V	K	D	Y	Y
	AAG	AGC	ACC	TCT	GGG	GGC	ACA	GCG	GCC	CTG	GGC	TGC	CTG	GTC	AAG	GAC	TAC
460	F	P	E	P	V	T	V	S	W	N	S	G	A	L	T	S	G
	TTC	CCC	GAA	CCG	GTG	ACG	GTG	TCG	TGG	AAC	TCA	GGC	GCC	CTG	ACC	AGC	GGC
511	V	H	T	F	P	A	V	L	Q	S	S	G	L	Y	S	L	S
	GTG	CAC	ACC	TTC	CCG	GCT	GTC	CTA	CAG	TCC	TCA	GGA	CTC	TAC	TCC	CTC	AGC
562	S	V	V	T	V	P	S	S	S	L	G	T	Q	T	Y	I	C
	AGC	GTG	GTG	ACC	GTG	CCC	TCC	AGC	AGC	TTG	GGC	ACC	CAG	ACC	TAC	ATC	TGC
613	N	V	N	H	K	P	S	N	T	K	V	D	K	K	A	E	P
	AAC	GTG	AAT	CAC	AAG	CCC	AGC	AAC	ACC	AAG	GTG	GAC	AAG	AAA	GCA	GAG	CCC
664	K	S	C	D	K	T	H	T	C	P	P	C	P	K	L	E	D
	AAA	TCT	TGT	GAC	AAA	ACT	CAC	ACA	TGC	CCA	CCG	TGC	CCA	AAG	CTT	GAA	GAT
	D	I	I	I	A	T	K	N	G	K	V	R	G	M	N	L	T

Figure 19 (continued)

715 GAC ATC ATA ATT GCA ACA AAG AAT GGA AAA GTC AGA GGG ATG AAC TTG ACA  
 V F G G T V T A F L G I P Y A Q P  
 766 GTT TTT GGT GGC ACG GTA ACA GCC TTT CTT GGA ATT CCC TAT GCA CAG CCA  
 P L G R L R F K K P Q S L T K W S  
 817 CCT CTT GGT AGA CTT CGA TTC AAA AAG CCA CAG TCT CTG ACC AAG TGG TCT  
 D I W N A T K Y A N S C C Q N I D  
 868 GAT ATT TGG AAT GCC ACA AAA TAT GCA AAT TCT TGC TGT CAG AAC ATA GAT  
 Q S F P G F G S E M W N P N T D  
 919 CAA AGT TTT CCA GGC TTC TTT GGA TCA GAG ATG TGG AAC CCA AAC ACT GAC  
 L S E D C L Y L N V I P A P K P  
 970 CTC AGT GAA GAC TGT TTA TAT CTA AAT GTA TGG ATT CCA GCA CCT AAA CCA  
 K N A T V L I W I Y G G F Q T G  
 1021 AAA AAT GCC ACT GTA TTG ATA TGG ATT TAT GGT GGT TTT CAA ACT GGA  
 T S S L H V Y D G K F L A R V E R  
 1072 ACA TCA TCT TTA CAT GTT TAT GAT GGC AAG TTT CTG GCT CGG GTT GAA AGA  
 V I V V S M N Y R V G A L G F L A  
 1123 GTT ATT GTA GTG TCA ATG AAC TAT AGG GTG GGT GCC CTA GGA TTC TTA GCT  
 L P G N P E A P G N M G L F D Q Q  
 1174 TTG CCA GGA AAT CCT GAG GCT CCA GGG AAC ATG GGT TTA TTT GAT CAA CAG  
 L A L Q W V Q K N I A A F G G N P  
 1225 TTG GCT CTT CAG TGG GTT CAA AAA AAT ATA GCA GCC TTT GGT GGA AAT CCT  
 K S V T L F G E S A G A A S V S L  
 1276 AAA AGT GTA ACT CTC TTT GGA GAA AGT GCA GGA GCT TCA GTT AGC CTG  
 H L L S P G S H S L F T R A I L Q  
 1327 CAT TTG CTT TCT CCT GGA AGC CAT TCA TTG TTC ACC AGA GCC ATT CTG CAA  
 S G S A N A P W A V T S L Y E A R  
 1378 AGT GGT TCC GCT AAT GCT CCT TGG GCG GTA ACA TCT CTT TAT GAA GCT AGG  
 N R T L N L A K L T G C S R E N E  
 1429 AAC AGA ACG TTG AAC TTA GCT AAA TTG ACT GGT TGC TCT AGA GAG AAT GAG  
 T E I I K C L R N K D P Q E I L L  
 1480 ACT GAA ATA ATC AAG TGT CTT AGA AAT AAA GAT CCC CAA GAA ATT CTT CTG  
 N E A A F V V P Y G T N L S V N F G

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Figure 19 (continued)

1531 AAT GAA GCA TTT GTT GTC CCC TAT GGG ACT AAT TTG TCA GTA AAC TTT GGT  
 P T V D G GAT TTT CTC ACT GAC ATG CCA GAC ATA TTA CTT GAA  
 1582 CCG ACC GTG GAT GAT TTT CTC ACT GAC ATG CCA GAC ATA TTA CTT GAA  
 L G Q F K K T Q I L V G V N K D E  
 1633 CTT GGA CAA TTT AAA AAA ACC CAG ATT TTG GTG GGT GAT AAA GAT GAA  
 G T A F L A Y G A P G F S K D N N  
 1684 GGG ACA GCT TTT TTA GCG TAT GGT GCT CCT GGC TTC AGC AAA GAT AAC AAT  
 S I I T R K E F Q E G L K I F P  
 1735 AGT ATC ATA ACT AGA AAA GAA TTT CAG GAA GGT TTA AAA ATA TTT TTT CCA  
 G V S E F G K E S I L F H Y T D W  
 1786 GGA GTG AGT GAG TTT GGA AAG GAA TCC ATC CTT TTT CAT TAC ACA GAC TGG  
 V D D Q R P E N Y R E A L G D V V  
 1837 GTA GAT GAT CAG AGA CCT GAA AAC TAC CGT GAG GCC TTG GGT GAT GTT GTT  
 G D Y N F I C P A L E F T K K F S  
 1888 GGG GAT TAT AAT TTC ATA TGC CCT GGC TTT GAG TTT ACC AAG AAG TTC TCA  
 E W G N N A F F Y Y F E H R S S K  
 1939 GAA TGG GGA AAT AAT GCC TTT TTC TAC TAT TTT GAA CAC CGA TCC TCC AAA  
 L P W P E W M G V M H G Y E I E F  
 1990 CTT CCG TGG CCA GAA TGG ATG GGA GTG ATG CAT GGC TAT GAA ATT GAA TTT  
 V F G L P L E R R D N Y T K A E E  
 2041 GTC TTT GGT TTA CCT CTG GAA AGA AGA GAT AAT TAC ACA AAA GCC GAG GAA  
 I L S R S I V K R W A N F A K Y G  
 2092 ATT TTG AGT AGA TCC ATA GTG AAA CGG TGG GCA AAT TTT GCA AAA TAT GGG  
 N P N E T Q N N S T S W P V F K S  
 2143 AAT CCA AAT GAG ACT CAG AAC AAT AGC ACA AGC TGG CCT GTC TTC AAA AGC  
 T E Q K Y L T L N T E S T R I M T  
 2194 ACT GAA CAA AAA TAT CTA ACC TTG AAT ACA GAG TCA ACA ATA ATG ACG  
 K L R A Q Q C R F W T S F F P K V  
 2245 AAA CTA CGT GCT CAA CAA TGT CGA TTC TGG ACA TCA TTT TTT CCA AAA GTC  
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2296 TGA

Figure 20

a-CD20 VL construct

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E I V L T Q S P G T L S L S P G E
1 GAA ATT GTG TTG ACG CAG TCT CCA GGC ACC CTG TCT TTG TCT CCA GGC GAA
R A T L S C R A S S S V P Y I H W
52 AGA GCC ACC CTC TCC TGC AGG GCC AGC TCA AGT GTA CCG TAC ATC CAC TGG
Y Q Q K P G Q A P R L L I Y A T S
103 TAC CAG CAG AAA CCT GGC CAG GCT CCC AGG CTC CTC ATC TAT GCC ACA TCC
A L A S G I P D R F S G S G T
154 GCT CTG GCT TCT GGC ATC CCA GAC AGG TTC AGT GGC AGT GGC TCT GGC ACA
D F T L T I S R L E P E D F A V Y
205 GAC TTC ACT CTC ACC ATC AGC AGA CTG GAG CCT GAA GAT TTT GCA GTG TAT
Y C Q Q W L S N P P T F G Q G T K
256 TAC TGT CAG CAG TGG CTG AGT AAC CCA CCC ACT TTT GGC CAG GGC ACC AAG
L E I K R T V A A P S V F I F P P
307 CTG GAG ATC AAA CGA ACT GTG GCT GCA CCA TCT GTC TTC ATC TTC CCG CCA
S D E Q L K S G T A S V V C L L N
358 TCT GAT GAG CAG TTG AAA TCT GGA ACT GCC TCT GTT GTG TGC CTG AAT
N F Y P R E A K V Q W K V D N A L
409 AAC TTC TAT CCC AGA GAG GCC AAA GTA CAG TGG AAG GTG GAT AAC GCC CTC
Q S G N S Q E S V T E Q D S K D S
460 CAA TCG GGT AAC TCC CAG GAG AGT GTC ACA GAG CAG GAC AGC AAG GAC AGC
T Y S L S S T L T L S K A D Y E K
511 ACC TAC AGC CTC AGC ACC CTG ACG CTG AGC AAA GCA GAC TAC GAG AAA
H K V Y A C E V T H Q G L S S P V
562 CAC AAA GTC TAC GCC TGC GAA GTC ACC CAT CAG GGC CTG AGC TCG CCC GTC
T K S S F N R G E C *
613 ACA AAG AGC TTC AAC AGG GGA GAG TGT TAG

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